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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/016,737	01/30/1998	GERALD P. MURPHY	NWBI135161	7366

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
05/12/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/016,737	MURPHY ET AL.	
	Examiner	Art Unit	
	KAREN CANELLA	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Please note that this application is now assigned to Examiner Karen Canella.

After review and reconsideration, the Election of Species Requirement of 6/4/99 is hereby withdrawn. Claims 25 and 27, previously withdrawn, are now included for examination with the claims 23, 24, 26 and 28-37. Claims 23-37 are pending and under consideration.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 121 and 365(c) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application No. 08/509,254 and PCT/US96/12389, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Claim 23 encompasses the subject matter of claims 25 and 27. Neither of the '254 or '389 application provide an adequate written description of the prostate antigens of SEQ ID NO:4-38 required by claims'25 and 27. Therefore neither of 'applications '254 or ''389 provide adequate support for the scope of independent claim 23. Further, claim 24 requires SEQ ID NO:3, wherein said sequence is X, L or M, XXXXX, V or L, which is also not supported by the '254 or '389 application which disclose only LXXXXXXV. Accordingly, the instant claims are not given benefit of the earlier filing dates of 7/29/1996 or 7/31/1995.

Claim 25 is objected to because of the following informalities: the improper recitation of a Markush group. Applicant is advised to amend the claim to recite VVHYRKWIK (SEQ ID NO:37) **and** CYASGWGSI (SEQ ID NO: 38). Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 is vague and indefinite in the recitation of wherein the human dendritic cells are immature dendritic cells because it is unclear if applicant is referring to the immaturity of the dendritic cells before or after exposure to the soluble prostate antigen, Il-4 and GM-CSF.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23, 24, 31-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Tjoa et al (The Prostate, 1995, Vol. 27, pp. 63-69, reference of the IDS submitted March 3, 2005).

Claim 23 is drawn to a composition comprising an isolated cell population having human dendritic cells, wherein said population has been cultured in the presence of GM-CSF and Il-4 and exposed in vitro to a soluble prostate antigen. Claim 24 embodies the composition of claim23 wherein the prostate antigen is a lysate of LNCap cells, a membrane prep of prostate tumor cells from a patient, PSMA, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, PSA or the prostate mucin antigen recognized by the PD41 antibody. Claim 31 embodies the composition of claim 23 wherein said dendritic cells can activate 2 to 3 fold more T cells recognizing the prostate antigen in comparison to dendritic cells cultured in GM-CSF and Il-4 that have not been

exposed to the prostate antigen in vitro. Claim 32 embodies the composition of claim 23 wherein the dendritic cells are immature. Claim 33 embodies the composition of claim 23 wherein the T cells are CD4+. Claim 34 embodies the composition of claim 23 wherein the T cells are CD8+. Claim 35 embodies the composition of claim 23 wherein the dendritic cells are isolated from a prostate cancer patient.

Tjoa et al disclose the culturing of dendritic cells isolated from prostate cancer patients in GM-CSF and Il-4 (page 64, "DC Culture"), and the pulsing of the cultured dendritic cells with a lysate of LNCap (page 47, legend for Figure 4). The peptide-pulsed dendritic cells of Tjoa et al fulfill the limitations of having an increased ability to activate T cells specific to the prostate antigen and compared to dendritic cells cultured in the same manner and not exposed to the soluble prostate antigen in the LnCAP lysate as evidenced by the graph of figure 4. The in vitro primed dendritic cells of Tjoa et al fulfill the limitations of claim 31 requiring dendritic cells having the ability to activate 2 to 3-fold more T cells specific to the prostate antigen and compared to dendritic cells cultured in the same manner and not exposed to the LnCAP lysate in vitro as evidenced by the graph of figure 4. The peptide pulsed dendritic cells of Salgaller et al fulfill the requirements of claims 32- 34 because they are made in the same manner as claimed and therefore have the same functional characteristics with respect to activation of T cells which are CD4+ and CD8+.

Claims 23, 24, 31-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Murphy et al (The Prostate, 1996, Vol. 29, pp. 371-380, reference of the IDS submitted December 2, 1998).

Murphy et al disclose the culturing of dendritic cells isolated from prostate cancer patients in GM-CSF and Il-4 (page 373, "DC Culture"), and the pulsing of the cultured dendritic cells with PSMA peptides (pages 374, "DC/Peptide-Pulsed DC") having the sequences of the instant SEQ ID NO:1 and SEQ ID NO:2 (pages 372-373, "Reagents and Cytokines"). The peptide-pulsed dendritic cells of Murphy et al fulfill the limitations of having an increased ability to activate T cells specific to the prostate antigen and compared to dendritic cells cultured in the same manner and not exposed to the PSMA peptide in vitro because said dendritic cells are made by the same method as that claimed. The peptide-pulsed dendritic cells of Murphy et al fulfill

the limitations of claim 31 requiring dendritic cells having the ability to activate 2 to 3-fold more T cells specific to the prostate antigen and compared to dendritic cells cultured in the same manner and not exposed to the PSMA peptide in vitro because said dendritic cells are made by the same method as that claimed. The peptide pulsed dendritic cells of Murphy et al fulfill the requirements of claims 32-and 34 because they are made in the same manner as claimed and therefore have the same functional characteristics with respect to activation of T cells which are CD4+ and CD8+.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 23, 24, 28-35 rejected under 35 U.S.C. 103(a) as being unpatentable over Tjoa et al (The Prostate, 1995, Vol. 27, pp. 63-69) in view of Makino and Baba (Scan J Immunol, 1997, Vol. 45, pp. 618-622).

Tjoa et al teach as set forth above. Tjoa et al do not teach the use of cryopreserved dendritic cells.

Makino and Baba teach a method of cryopreserving dendritic cells from PBMC prior to exposure of said dendritic cell to a target antigen (page 619 under "Production of DC"). Makino and Baba teach that the cryopreserved PBMC provided DC or DC-precursors as efficiently as

fresh PBMC (page 620 under "comparison of cryopreserved and freshly isolated PBMC as a source of DC"). Makino and Baba teach that established dendritic cells were also preserved by the same method and retained their viability (page 621, second column, lines 7-8). Makino and Baba teach that the cryopreservation method is advantageous because it allows for the production of APC without the need for fresh PBMC (page 621, second column, lines 1-6).

It would have been prima facie obvious at the time that the claimed invention was made to use cryopreserved PBMC as a source for dendritic cells in the method of Tjoa et al . One of skill in the art would have been motivated to do so by the teachings of Makino and Baba on the retention of DC precursors in cryopreserved PBMC, and the advantage of not having to drawn fresh blood at the time of the experiment using the method of Tjoa et al.

Claims 23, 24, 28-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murphy et al (The Prostate, 1996, Vol. 29, pp. 371-380) in view of Makino and Baba (Scan J Immunol, 1997, Vol. 45, pp. 618-622)..

Murphy et al teach as set forth above. Murphy et al do not teach the use of cryopreserved dendritic cells.

Makino and Baba teach a method of cryopreserving dendritic cells from PBMC prior to exposure of said dendritic cell to a target antigen (page 619 under "Production of DC"). Makino and Baba teach that the cryopreserved PBMC provided DC or DC-precursors as efficiently as fresh PBMC (page 620 under "comparison of cryopreserved and freshly isolated PBMC as a source of DC"). Makino and Baba teach that established dendritic cells were also preserved by the same method and retained their viability (page 621, second column, lines 7-8). Makino and Baba teach that the cryopreservation method is advantageous because it allows for the production of APC without the need for fresh PBMC (page 621, second column, lines 1-6).

It would have been prima facie obvious at the time that the claimed invention was made to use cryopreserved PBMC as a source for dendritic cells in the method of Tjoa et al . One of skill in the art would have been motivated to do so by the teachings of Makino and Baba on the retention of DC precursors in cryopreserved PBMC, and the advantage of not having to drawn fresh blood at the time of the experiment using the method of Murphy et al.

Claims 23, 24, 26, 31, 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murphy et al (The Prostate, 1996, Vol. 29, pp. 371-380) in view of Paglia et al (Journal of Experimental Medicine, 1996, vol. 183, pp. 317-322).

Claim 26 embodies the method of claim 23 wherein the dendritic cells are extended life-span dendritic cells.

Murphy et al teach as set forth above. Murphy et al teach that patients received four or five doses at 6-8 week intervals during the study period (page 373, "Treatment Groups"). Murphy et al do not teach the use of extended life-span dendritic cells.

Paglia et al teach that immortalized dendritic cell line primed in vitro to a soluble antigen elicits a cytotoxic immune response to that antigen in vivo (page 318 under "Cell Lines" and page 319, firs paragraph under "Results").

It would have been prima facie obvious at the time that the claimed invention was made to use immortalized dendritic cells in the method of Murphy et al. One of skill in the art would have been motivated to do so by the teachings of Paglia et al regarding the ability of immortalized dendritic cells to retain antigen-presenting function in vivo. One of skill in the art would also understand that using immortalized dendritic cells from a patient would allow for the establishment of a dendritic cell culture prior to the treatment of the patient and provide for uniform populations of peptide-pulsed dendritic cells to be administered back into the patient.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23, 24, 26, 28-37 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 5,788,963 in view of M. Lotze, Annals of Surgery, 1997, vol. 226, pp. 1-5).

The claims of the '963 patent teach the instant composition with the exception that the claims do not specify that the dendritic cells are from a culture including GM-CSF and Il-4.

Lotze teaches that dendritic cells cultured in GM-CSF and Il-4 are capable of eliciting therapeutic effects against tumors (page 3, first column, lines 14-17 and page 4, first column, lines 18-22).

It would have been prima facie obvious at the time that the claimed invention was made to use dendritic cells cultured with GM-CSF and Il-4 in the method of the '963 patent. One of skill in the art would have been motivated to do so by the teachings of Lotze on the ability of dendritic cells cultured with GM-CSF and Il-4 to elicit anti-tumor therapeutic effects.

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Claims 23-37 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No. 11/972,565 in view of. M. Lotze, Annals of Surgery, 1997, vol. 226, pp. 1-5)

The claims of the '565 application teach the instant composition with the exception that the claims do not specify that the dendritic cells are from a culture including GM-CSF and Il-4.

Lotze teaches that dendritic cells cultured in GM-CSF and Il-4 are capable of eliciting therapeutic effects against tumors (page 3, first column, lines 14-17 and page 4, first column, lines 18-22).

It would have been prima facie obvious at the time that the claimed invention was made to use dendritic cells cultured with GM-CSF and Il-4 in the method of the '565 patent. One of skill in the art would have been motivated to do so by the teachings of Lotze on the ability of dendritic cells cultured with GM-CSF and Il-4 to elicit anti-tumor therapeutic effects.

This is a provisional obviousness-type double patenting rejection.

Claims 23, 24, 31-37 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6-11 of copending Application No. 12/096,419. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '419 application anticipate the instant claims to the extent that the dendritic cells are contacted with a cell lysate of a tumor cell which is a prostate tumor (claims 2-4); the tumor cells are from a patient (claim 11); the dendritic cells are contacted with GM-CSF and Il-4 (claims 6 and 9); the dendritic cells are from dendritic cell precursors for a patient or from a HLA-matched individual (claim 11.) or the patient (claim 11).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

All claims are rejected.

All other rejections and objections as set forth or maintained in the prior office action are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAREN CANELLA whose telephone number is (571)272-0828. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu can be reached on (571)272-0839. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643